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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,395	07/10/2001	Keith D. Allen	R-653	9465

7590 11/24/2003

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/903,395	ALLEN, KEITH D.
	Examiner	Art Unit
	Michael C. Wilson	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *1-7,9,10,13-16,27,29 and 33-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,11,12,17-26,28 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11-21-01*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group III, claims 8, 11, 12, 17-26, 28 and 30-32, filed 7-22-03 is acknowledged.

Claims 1-7, 9, 10, 13-16, 27, 29 and 33-37 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Specification

The specification is objected to because the first line of the specification should state the application claims priority to US Provisional Application No: 60/218,074, filed 7-12-00 and 60/243,958, filed 10-26-00.

The application numbers throughout the specification will require updating as necessary.

The description of Fig. 2A-2B should clearly state the sequence shown is SEQ ID NO:1.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 8, 11, 12, 17-26, 28 and 30-32 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility.

Claims 8, 17-26 and 28 are directed toward a non-human transgenic animal, specifically a mouse, having a disruption of an MC3-R gene. Claims 11, 12 and 30-32 are directed toward using a non-human transgenic animal, specifically a mouse, having a disruption of an MC3-R gene. The specification teaches making MC3-R -/- mice having only one kidney (pg 54, line 5-10). However, the strain of mice used spontaneously has only one kidney (pg 54, line 8). Therefore, the specification states it cannot be determined whether the lack of a kidney correlates to the disruptions in MC3-R (pg 54, lines 9-10). As such, a mouse with only one kidney does not have a use as claimed because it is not caused by the disruption in MC3-R or represent a disease state caused by a disruption in MC3-R. The specification suggests using the mice as a model of disease, specifically as a model for behavioral abnormalities, such as neurological, neuropsychological, psychotic phenotypes (pg 19-21; pg 21, lines 6-10). However, the specification does not disclose that behavioral abnormalities, specifically neurological, neuropsychological or psychotic disease found in humans, are linked to a disruption in MC3-R. Male MC3-R -/- mice were passive, hypoactive and did not attempt to escape during examination. Female MC3-R -/- mice were unremarkable (pg 54, lines 13-15). The specification does not provide any use for such a mouse, how such a mouse correlates to any disease, or that a disruption in MC3-R is found in hypoactive humans. None of the phenotypes described on pg 54 or claimed correlate

to a useful phenotype because the phenotypes are not specific to a disease and are not linked to a disruption in an MC3-R gene in humans. The results of the tests are also not statistically significant because the number of mice tested is not disclosed. The mice claimed cannot be used to determine compounds that modulate MC3-R expression (e.g. claim 11) because MC3-R is not expressed in the mice. Using the mice to determine whether a particular phenotype is ameliorated is not a specific or substantial utility because the specification does not link the phenotype to any specific disease or to a disease caused by a disruption in humans. The specification does not identify any compounds that ameliorate any condition using the mice. Thus, the specification does not provide a specific or substantial use for a mouse as claimed, specifically having a behavioral or renal abnormality as claimed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 11, 12, 17-26, 28 and 30-32 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use mice having a disruption in an MC3-R gene and a behavioral or renal abnormality.

The specification does not teach how to make animals or cells having a disruption in an MC3-R gene other than mice. The only means of making a non-human animal with a disruption in an MC3-R gene taught in the specification is by using mouse embryonic stem cell technology. The state of the art at the time of filing was such that embryonic stem (ES) cell technology had only been successful in mice. Wagner (May 1995, Clin. and Experimental Hypertension, Vol. 17, pages 593-605) and Mullins (1996, J. Clin. Invest., Vol. 98, pages S37-S40) taught germline transmission of ES cells has not been demonstrated in species other than mice and the growth of ES cells from species other than mice is unreliable. Wall (1996, Theriogenology, Vol. 45, pg 57-68) taught transgene expression and the physiological result of such expression in livestock was not always accurately predicted in transgenic mice (page 62, line 7). Since the time of filing, Zan (Nature Biotech, 2003, Vol. 21, pg 645-651) taught making knockout rats using mutagenized male rats, which was not taught in the specification and considered essential to making knockout rats. The specification fails to provide sufficient guidance to make transgenics other than mice by teaching obtaining ES cells in species other than mice. The specification does not teach the nucleic acid sequence of an MC3-R gene in non-mice, non-human species or correlate the MC3-R gene in mice to the MC3-R gene in other species. The specification does not teach how to make knockout animals other than mice or correlate making knockout mice to other species. Therefore, the specification does not provide adequate guidance for one of skill in the art to make a transgenic, non-human animal or cells having a disruption in an MC3-R gene in any species other than mice.

The specification does not provide adequate correlation between the phenotype obtained in mice to the phenotype obtained in other species. The state of the art at the time of filing was that the phenotype of transgenic mice does not predict the phenotype in non-mice species. Models of human diseases have relied on transgenic rats when the development of transgenic mice having the desired phenotype was not feasible. Mullins (1990, Nature, Vol. 344, pg 541-544) produced outbred Sprague-Dawley x WKY rats with hypertension caused by expression of a mouse Ren-2 renin transgene. Hammer (1990, Cell, Vol. 63, pg 1099-1112) describes spontaneous inflammatory disease in inbred Fischer and Lewis rats expressing human class I major histocompatibility allele HLA-B27 and human b_2-microglobulin transgenes. Both investigations were preceded by the failure to develop human disease-like symptoms in transgenic mice (Mullins, 1989, EMBO, Vol. 8, pg 4065-4072; Taurog, 1988, J. Immunol., Vol. 141, pg 4020-4023) expressing the same transgenes that successfully caused the desired symptoms in transgenic rats. Therefore, the specification does not enable making transgenic having the disclosed phenotypes in species other than mice.

In addition, claims 17-26 do not provide a nexus between the disruption in MC3-R and the phenotypes claimed. The claims do not recite the disruption of MC3-R causes the phenotype claimed. The specification does not teach disrupting the MC3-R gene in mice already lacking production of MC3-R or in mice already having the phenotypes recited in claims 17-26. Given the art of transgenics at the time of filing taken with the guidance provided in the specification, the claim should reflect the fact that the phenotypes recited in claims 17-26 are a result of MC3-R disruption.

Otherwise, it would require one of skill undue experimentation to make the mouse as broadly claimed.

The specification does not enable using a transgenic with a wild-type phenotype as encompassed by claims 8, 11, 12, 28 and 30-32. The transgenics in the claims do not recite any phenotype and may, therefore, have any phenotype including wild-type phenotype. In particular, claims 30-32 only require determining whether a phenotype is present and do not require the mouse used has the phenotype. The specification does not provide any use for a transgenic having a disruption in an MC3-R gene that has a wild-type phenotype. The only disclosed phenotype for the transgenic claimed is one that correlates to a disruption in an MC3-R gene. Therefore, the claims should recite a non-wild-type phenotype that correlates to a disruption in an MC3-R gene.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 11, 12, 17-26, 28, 30-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of what applicants consider "MC3-R" genes cannot be determined. The specification defines the term as any gene of SEQ ID NO:1 or having homology to SEQ ID NO:1 (pg 8, lines 7-12). However, not all genes sharing homology with SEQ ID NO:1 are MC3-R genes. For example MC4-R shares homology with SEQ ID NO:1, and is not an MC3-R gene.

Claims 17-26 are indefinite because they do not clearly set forth that the disruption in MC3-R causes the phenotype.

Claim 21 is indefinite because if the decrease in initiative ("passivity") is over a period of time or in comparison to a wild-type control.

The metes and bounds of what applicants consider "hypoactivity" cannot be determined (claim 22). The phrase is not defined in the specification and does not have an art recognized definition. The metes and bounds of what applicants consider "hypoactive" cannot be determined. How active is hypoactive?

Claim 23 is indefinite because if the decrease is over a period of time or in comparison to a wild-type control.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 8, 11, 12, 17-26, 28 and 30-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Butler (Sept. 2000, Endocrinology, Vol. 141, pg 3518-3521).

Provisional application 60/218,074 suggested a mouse having a disruption in SEQ ID NO:1 but did not teach the phenotype of the mouse. Specifically '074 did not teach that the mouse was passive, hypoactive or did not attempt to escape while being handled. As such, '074 supports claims 8 and 28, but not claims 17-26. The effective

filing date of claims 17-26 as they relate to obtaining a mouse that was passive, hypoactive or did not attempt to escape while being handled is 10-26-00, the filing date of 60/243,958, which taught male homozygous mice were passive, hypoactive and did not attempt to escape while being handled (pg 69, last 3 lines). The effective filing date of claims 17-26 as they relate to having a kidney abnormality, reduced kidney size, unilateral renal agenesis, and decreased locomotion is the instant application, filed 7-10-01 because such limitations are not taught in the provisional applications.

Butler taught male mice with a homozygous disruption in the MC3-R gene had reduced energy expenditure as determined by reduced wheel running behavior (pg 3520, col. 1, last full ¶). Reduced wheel running is considered hypoactive and passive as claimed. The mice taught by Butler inherently do not attempt to escape and have the kidney abnormalities claimed because they were made using the method described in the specification. The disruption of the MC3-R gene in Butler is the same disruption disclosed in the instant application. Therefore, the phenotypes claimed are inherent in the mouse of Butler because the mouse of Butler has the same structure disclosed in the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8, 11, 12, 28 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huszar (Cell, Jan. 10, 1997, Vol. 88, pg 131-141) in view of Desarnaud (1994, Biochem. J., Vol. 299, pg 367-373).

Huszar taught making a mouse having a disruption in MC4-R gene. Huszar did not teach disrupting the MC3-R gene.

However, Desarnaud taught the nucleic acid sequence of the mouse MC3-R gene.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a transgenic mouse having a disruption in melanocortin gene as taught by Huszar wherein the melanocortin gene was MC3-R as taught by Desarnaud. One of ordinary skill in the art at the time the invention was made would have been motivated to disrupt the MC3-R gene instead of the MC4-R gene to determine the function of MC3-R *in vivo*.

Thus, Applicants' claimed invention, as a whole is prima facie obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

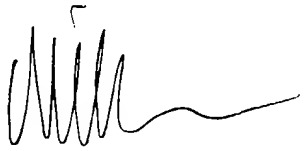
Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120. The examiner's phone number will change on Jan. 12th, 2004 to 571-272-0738.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER